URINARY INCONTINENCE

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LEARNING OBJECTIVES:

- Given a clinical presentation, make a diagnosis of urgency, stress or mixed incontinence and list the risk factors pertinent to a diagnosed of incontinence
- In a patient presenting with urinary incontinence
  - List the recommended initial evaluation for each type of incontinence
  - List the ancillary testing that can be necessary in certain situations
- In a patient presenting with urgency incontinence,
  - Name the different 1st, 2nd and 3rd line therapy options
  - Describe the mechanism of action of these treatment modalities
  - List the potential side effects and contraindications of these treatments
- In a patient with stress incontinence
  - Name the different treatment options
  - Select the possible treatment options for specific indications

I. Types of urinary incontinence

Urinary incontinence is defined as the complaint of any involuntary loss of urine. The prevalence of incontinence in women increases with age. It has been estimated that 25-45% of women suffer from any type of urinary incontinence. Older women are more likely to have mixed and urgency incontinence and younger and middle-aged women typically report stress incontinence.
When evaluating a patient with urinary incontinence, it is extremely important to identify the type of incontinence, the degree of bother, the frequency and the severity, the social impact and the impact on the patient's quality of life.

A. Classification and terminology

Urinary incontinence is classified as followed:

Urgency urinary incontinence (UUI) is the complaint of involuntary leakage accompanied by or immediately preceded by urgency.
Patients with UUI usually complain of symptoms of urgency, frequency and nocturia,

> **Urgency** is the complaint of a sudden, compelling desire to pass urine, which is difficult to defer. This refers to a pathologic condition unlike the "normal" urge to void.
> **Increased urinary frequency or frequency** is the complaint that micturition occurs more frequently during waking hours than previously deemed normal by the patient. Traditionally, up to 7 voids per waking hours is considered normal.
> **Nocturia** is the complaint of interruption of sleep one or more ties because of the need to micturate. Each void is preceded and followed by sleep. Many disorders other than bladder issues can lead to nocturia.

Stress urinary incontinence (SUI) is the complaint of involuntary leakage on effort or exertion, or on sneezing or coughing.

Mixed Urinary Incontinence is the complaint of involuntary leakage associated with urgency and also with effort, exertion, sneezing and coughing. A lot of patients suffer from mixed symptoms.

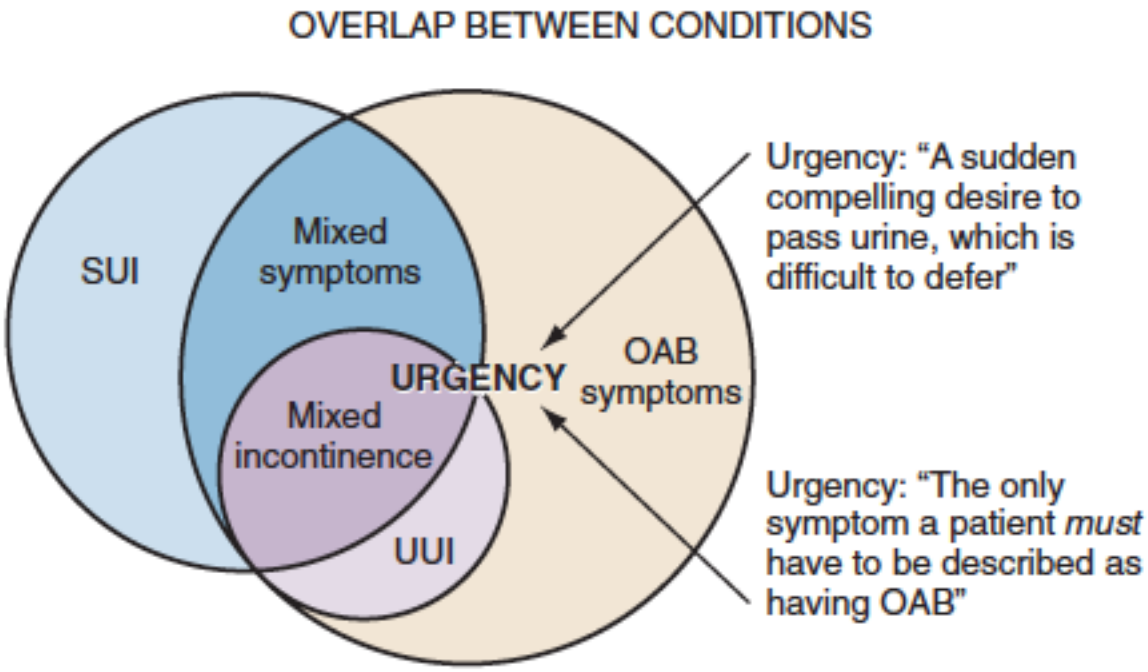

Figure 1. Overlap between urinary symptoms and types of incontinence, Campbell Walsh Urology 10th edition, 2012

Although sometimes referred as another type of urinary incontinence, **Overflow incontinence** is not classified as a type of incontinence per the International Continence Society. Overflow incontinence occurs when the bladder does not empty completely, causing leakage when the bladder becomes overly full. Evaluation and treatments should focus on the causes and improvement of bladder emptying.

When evaluating a patient with UI, it is extremely important to differentiate the type of incontinence the patient is complaining about or which type is more bothersome, because causes and treatments are different.

Types of urinary incontinence

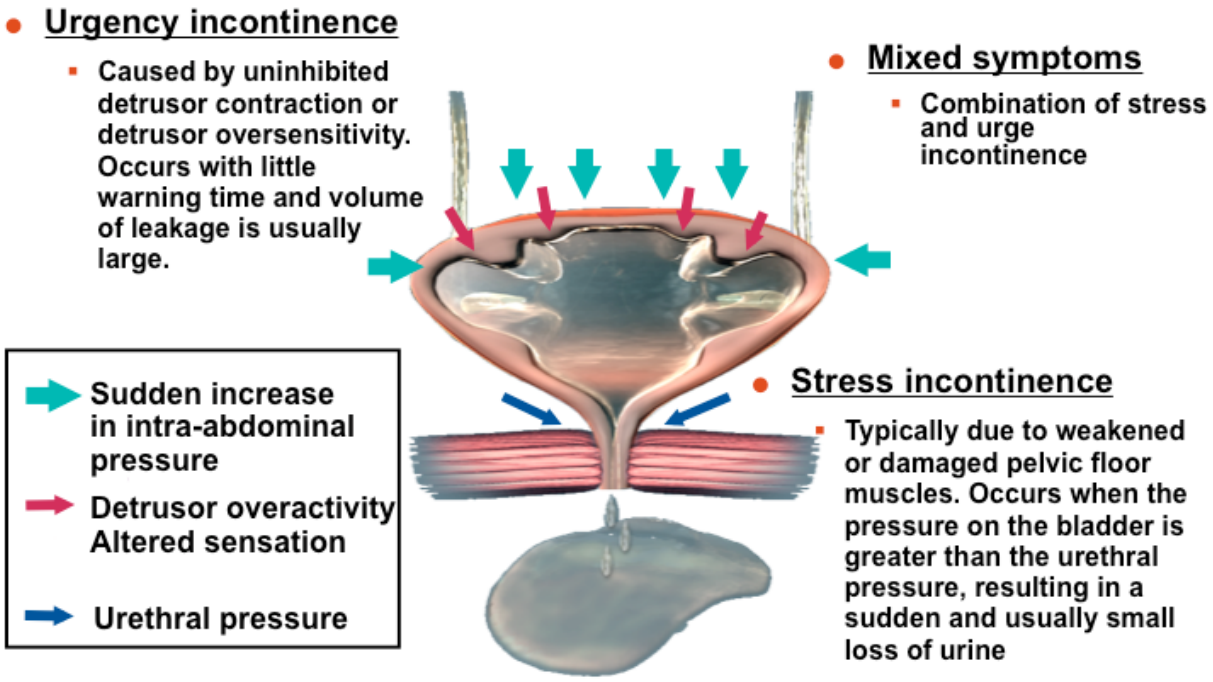

Figure 2. Types of urinary incontinence

B. Incontinence screening questionnaires

In order to help physicians differentiate which type of incontinence patients suffer from, several questionnaires have been developed to screen and assess degree of bother. One of the most commonly used is the Urogenital Distress Inventory short form (UDI-6). This questionnaire is very useful to assess the presence of frequency and urgency incontinence symptoms (#1 and #2), SUI (#3 and #4), obstructive voiding symptoms (#5) and presence of pain (#6).

Urogenital Distress Inventory short form (UDI-6)

Do you experience and, if so, how much are you bothered by:

		Not at all	A little bit	Moderately	Greatly
#1	Frequent urination	0	1	2	3
#2	Urine leakage related to urgency	0	1	2	3
#3	Urine leakage related to physical activity	0	1	2	3
#4	Small amounts of urine leakage	0	1	2	3
#5	Difficulty emptying your bladder	0	1	2	3
#6	Pain or discomfort in the lower abdomen/genitalia	0	1	2	3

Another questionnaire frequently used but in this case, to evaluate the impact of the incontinence on quality of life and activities is the Incontinence Impact Questionnaire short form (IIQ-7).

Incontinence Impact Questionnaire– Short Form IIQ-7

Some people find that accidental urine loss may affect their activities, relationships, and feelings. The questions below refer to areas in your life that may have been influenced or changed by your problem. For each question, circle the response that best describes how much your activities, relationships, and feelings are being affected by urine leakage.
Has urine leakage affected your...

	Not at All	Slightly	Moderately	Greatly
1. Ability to do household chores (cooking, housecleaning, laundry)	**0**	**1**	**2**	**3**
2. Physical recreation such as walking, swimming, or other exercise?	**0**	**1**	**2**	**3**
3. Entertainment activities (movies, concerts, etc.)?	**0**	**1**	**2**	**3**
4. Ability to travel by car or bus more than 30 minutes from home?	**0**	**1**	**2**	**3**
5. Participation in social activities outside your home?	**0**	**1**	**2**	**3**
6. Emotional health (nervousness, depression, etc.)?	**0**	**1**	**2**	**3**
7. Feeling frustrated?	**0**	**1**	**2**	**3**

Items 1 and 2 = physical activity
Item 5 = social/relationships
Items 3 and 4 = travel
Items 6 and 7 = emotional health

Scoring. Item responses are assigned values of 0 for "not at all," 1 for "slightly," 2 for "moderately," and 3 for "greatly." The average score of items responded to is calculated. The average, which ranges from 0 to 3, is multiplied by 33 1/3 to put scores on a scale of 0 to 100.

C. Risk factors for urinary incontinence
Several conditions have been found to be risk factors for the development of urinary incontinence:

- Age: SUI predominates in younger and middle-aged women, urgency and mixed incontinence are more common in older women
- Pregnancy and parity: associated with SUI
- Being pregnant: reported by most women at some time during pregnancy, usually in the third trimester.
- Number of vaginal deliveries: associated with SUI
- Large Birth Weight: associated with SUI
- Prolonged labor: associated with SUI
- Diet: alcohol, caffeine, carbonated beverage, bladder irritants, total fluid intake can worsen UI
- Obesity: well established as a factor that can cause both UUI and SUI. Weight reduction is associated with partial remission or complete resolution of UI.
- Diabetes
- Depression: can lead to UI and UI can lead to depression
- Race: lower prevalence of SUI in black and Asian compared with white women
- Genetics: 2-3X greater prevalence of SUI among first degree relatives of women with SUI

- Impaired physical function/impaired mobility
- Cognitive impairment

II. Urgency Urinary Incontinence.

A. Epidemiology of urgency urinary incontinence

Urgency urinary incontinence is considered part of what is commonly called "Overactive bladder syndrome" (OAB). UUI affects over 33 million people (16.6% of population). The prevalence increases with age, affecting around 10% of patients <45 years old and >30% of patients >65 years old. Among these, it is estimated that 63% are "OAB dry" (frequency and urgency without incontinence) and 37% are OAB wet (frequency and urgency with incontinence). OAB significantly impairs health related quality of life, even in those without urge incontinence.

B. Evaluation of urgency incontinence

OAB is a clinical diagnosis characterized by the presence of bothersome urinary symptoms. It is defined as urinary urgency that is usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of urinary tract infection or other obvious pathology.
The diagnosis of OAB syndrome should be made based on the self reported symptoms of urgency, frequency and/or urgency incontinence in the absence of other obvious process. A presumptive diagnosis of OAB can be made on the basis of the patient's history, an assessment of the symptoms, a physical examination, and urinalysis. Initiation of noninvasive treatment may not require an extensive further workup, such as behavioral therapy and drug therapy.

1. History
Important elements to obtain from the patient's history are the presence of OAB symptoms and degree of bother, presence of SUI symptoms, difficulty emptying, hesitancy, fluid intake habits, caffeine and alcohol intake, medications.
Other comorbidities that can cause, impact or change treatment options need to be identified.

-Neurologic diseases: Multiple Sclerosis, Spinal cord injury, Parkinson's disease, history of stroke. These diseases causes neurogenic bladder and most often associated with UUI.
-Mobility issues
-Fecal motility disorders: constipation or fecal incontinence
-Diabetes mellitus
-Prior incontinence/prolapse surgery
-Pelvic cancer
-Prior pelvic radiation

Other causes of OAB need to be excluded or treated before making the diagnosis of OAB and these include:
-bladder cancer/carcinoma in situ
-bladder outlet obstruction
-Pelvic organ prolapse
-polydipsia,
-diabetes insipidus,
-Interstitial cystitis/painful bladder syndrome,
-uncontrolled/untreated diabetes,
-sleep obstructive apnea (for nocturia)

-sleep disturbances
-medication induced frequency/urgency

If any of these diagnoses are suspected, additional workup is recommended.

2. Physical Examination:
Physical examination including a pelvic examination should be performed to assess the presence of pelvic organ prolapse, urethral diverticulum, atrophic vaginitis, perineal sensation, pain and suprapubic distension.

3. Urinalysis:
The main role of the urinalysis is to rule out the presence of UTI and of hematuria. If microscopic hematuria is found (defined as >3 RBC/field on microscopy), urologic evaluation is indicated to excluded the presence of stones and urothelial cancer. Urine culture is NOT necessary unless there are signs of infection on urinalysis.

4. Additional testing as needed:
-Post-void residual: should be assessed in patients with obstructive symptoms, history of incontinence surgery, neurologic diseases and at the clinician discretion when PVR assessment is deemed necessary. It can be obtain using US bladder scan or urethral catheter immediately after a patient voids.

-Urinary diaries: intake and voiding diary may be useful in patients who cannot describe their intake or voiding pattern or when inadequate fluid intake is suspected. It is typically recorded during a period of 3 days. Time of void, voided volume, volume, time and type of fluid intake, circumstance of incontinence episode and degree of urgency is typically recorded.

-Cystoscopy, imaging, urodynamic testing: not indicated in the initial workup of the uncomplicated patient. This should be obtained when patient are refractory or failed first line treatment options, when presence of GU neoplasia is suspected, intravesical foreign body or presence of bladder outlet obstruction.

C. Management of urgency incontinence

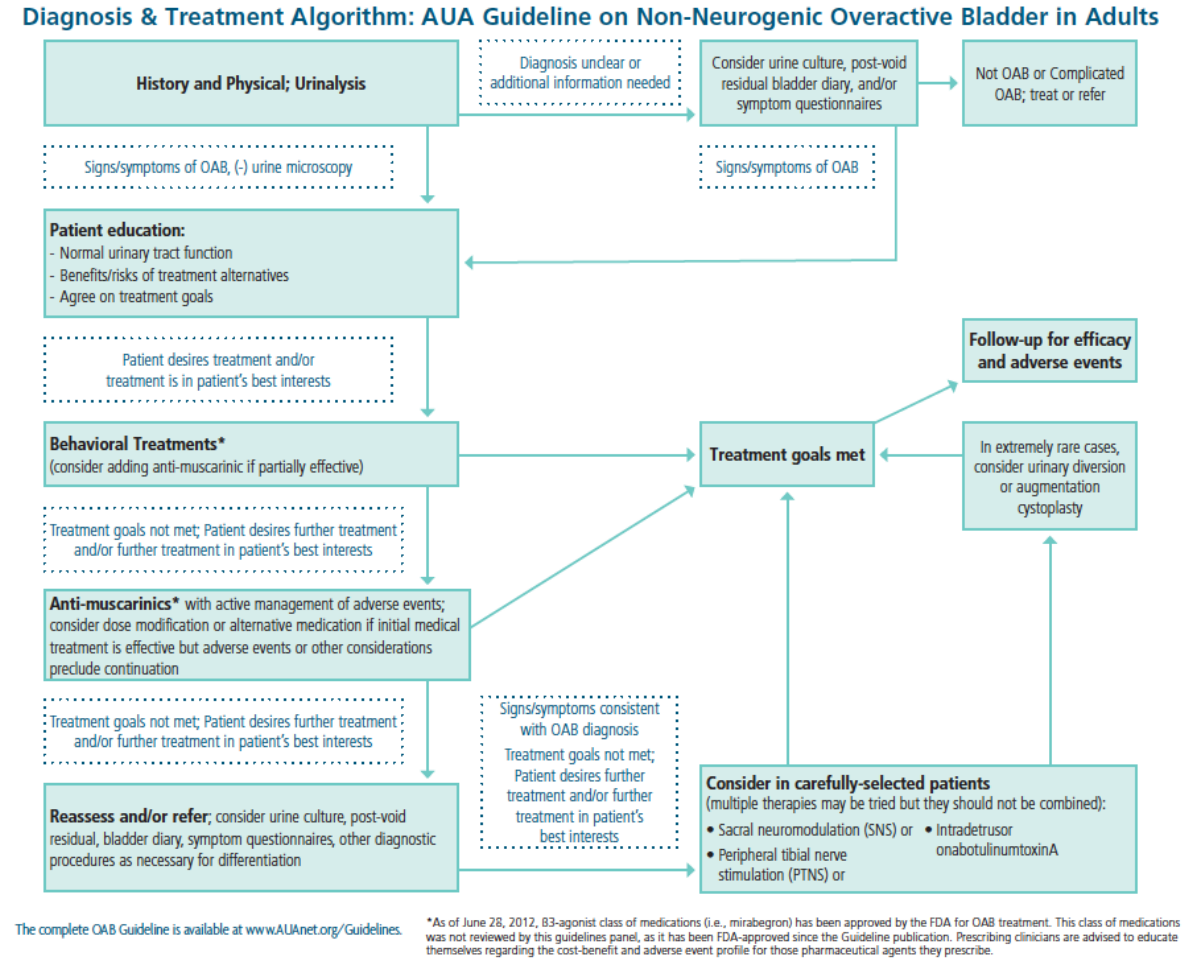

Figure 3. AUA guideline diagnosis and treatment algorithm of non-neurogenic overactive bladder in adults. 2012

1. Behavioral treatments

Behavioral treatment presents no risk to patients and should be offered to all.

- Education: patient should educated on normal and abnormal bladder function and "normal" fluid intake.
    - Total fluid intake per day should be limited to 1.5-2L
    - Total caffeine intake should be limited to 1-2 beverages
    - Limit fluid intake in the evening
    - Intake of other bladder irritants (nicotine, alcohol, citrus, spicy food, artificial sweeteners…) should also be limited
- Constipation should be treated.
- Modifying voiding habits: patient should be educated on bladder training. In some patients, this can take the form of "time-voiding", where patient is asked to go to the bathroom q 2-4 hours, especially when urgency is associated with infrequent voiding, or delayed voiding, where patient is asked to progressively increase the time between urination.
- Pelvic floor muscle training: much more successful if trained by a nurse or pelvic floor therapist, urge suppression techniques can be very effective in decreasing frequency and urgency and increasing bladder capacity.
- Weight loss: studies have confirmed that weight loss significantly reduces the number of UUI episodes.

2. Pharmacological treatments:

a. Anti-muscarinics/Anticholinergics

Anti-muscarinic agents have several commonly accepted mechanisms of action with respect to the treatment of OAB. Anti-muscarinic agents block binding of acetylcholine to muscarinic receptors on the smooth muscle membrane of the bladder. By doing so, they stabilize bladder smooth muscle, making it relatively refractory to the stimulation via parasympathetic neural impulses. Through this mechanism, anti0muscarinic therapy decreases the frequency of involuntary bladder contractions.

Anti-muscarinic therapy also increases bladder capacity and delays the initial urge to void. These actions suggest that anti-muscarinics may have effects on the filling/storage phase of the micturition cycle, not just the emptying phase.

Muscarinic receptors are found everywhere in the body. Even though the M2 receptor is found in higher proportion in the bladder, the ACH-major excitatory mechanism in the bladder is mediated by M3 receptors. The mechanism of action of anticholinergic medication for OAB is via its selectivity for the M3 receptors in the bladder. The side effects experienced with these medications are secondary to its effect on M1 or M2 or M3 receptors elsewhere in the body.

Oxybutynin, Tolterodine, Trospium, Solifenacin, Darifenacin, Fesoterodine are all anti-muscarinic agents approved for the treatment of OAB. No agent has been found to have superior efficacy. Their side effect profiles differ from their degree of selectiveness to the bladder M3 receptor. Anti-muscarinic agents have a high discontinuation rate secondary to the side effects.

Side effects of antimuscarinic agents
Dry mouth
Constipation
Dry-itchy eyes
Blurry vision
Dyspepsia
Impaired cognitive function

Absolute contraindication: antimuscarinic are contraindicated in patients with narrow angle glaucoma.

b. Beta-3-adrenergic agonist

Beta-3-adrenergic agonists are a new class of medication for the treatment of OAB. The stimulation of beta-3-adrenoreceptors relaxes the detrusor smooth muscle during storage to increase capacity. It reduces the occurrence of side effects related to M3 receptors. Only medication currently approved is Mirabegron. The efficacy is similar to antimuscarinics.

This class of medication has minimal anticholinergic type side effects. There has been a small rate of hypertension associated with this medication; therefore it should be avoided in patients with poorly controlled or untreated hypertension.

3. Third-line therapy – Refractory OAB treatment options

There are currently 3 treatment options approved for OAB refractory to behavioral and pharmacologic treatments.

a. Percutaneous Tibial Nerve Stimulation

This is an outpatient office procedure. Electric stimulation is delivered via a 34G needle electrode inserted medial and above the medical malleolus. The impulse is delivered to the posterior tibial nerve and travel from the ankle along the tibial nerve to the sacral nerves. The tibial nerve has input from S2, 3 and 4 roots, which is also the location of the sacral micturition center. This treatment requires 12 weekly sessions of 30 minutes each. If patient is improved at the end of 12 weeks, it requires "maintenance" therapy which is typically done once per month.
No significant side effect or complication has been reported.

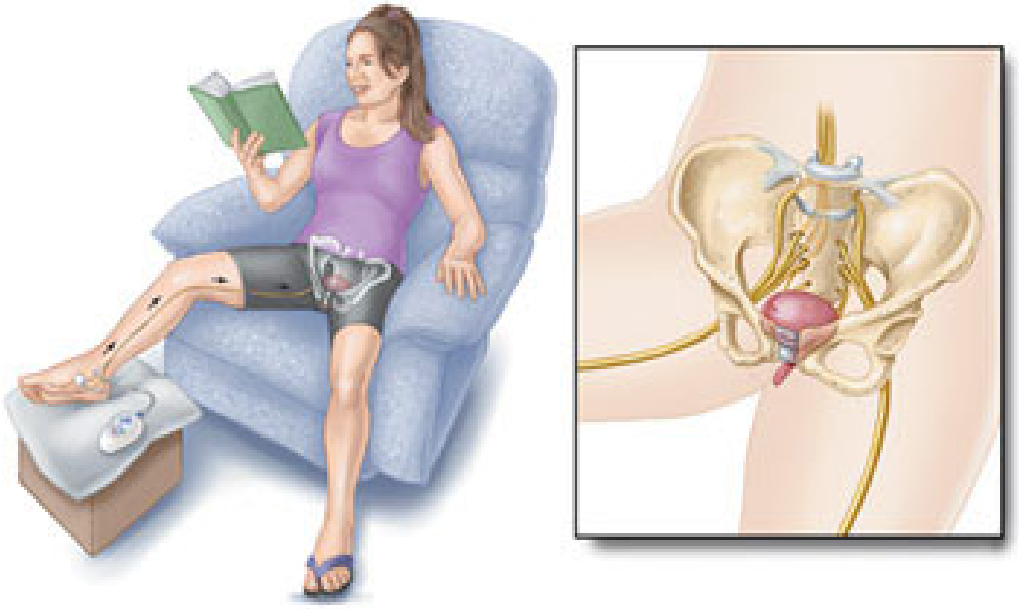

Figure 4. Posterior Tibial Nerve Stimulation. Cogentix medical, 2016

b. OnabotulinumtoxinA injection
Botulinum toxin is a neurotoxin produced by Clostridium botulinum. It binds to peripheral cholinergics terminals and inhibits the release of acetylcholine at the neuromuscular junction to cause muscle paralysis. It also inhibits afferent neurotransmitters, neuropeptides and sensory neurotransmission.

It was approved by the FDA in 2012 for the treatment of neurogenic detrusor overactivity and in 2013 for the treatment of urgency, frequency and urgency incontinence.

The injection is typically performed in the office under local anesthesia under cystoscopy. The product is diluted in 10-20cc and injected in 10-20 sites into the detrusor muscle.

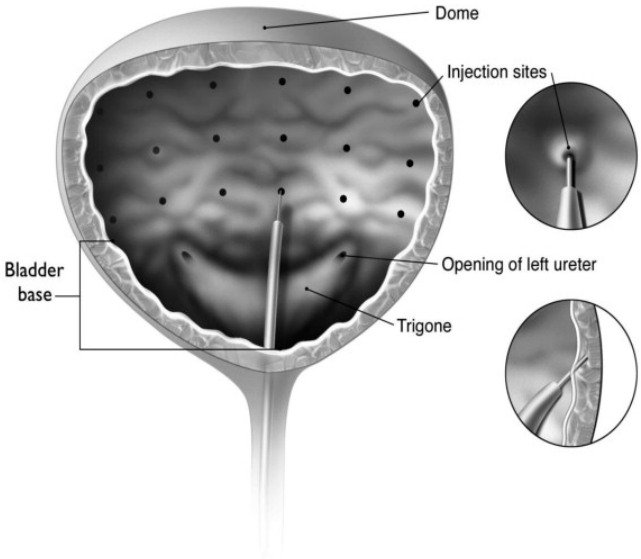

Figure 5. Injection protocol for detrusor botulinum toxin injection, Allergan 2016

The main complication/side effect reported from this treatment is the incidence of incomplete emptying/urinary retention requiring the patient to start to perform self-intermittent catheterization. It has been reported in 5-10% in the idiopathic OAB population. This usually resolves by 6 weeks after the injection. Injections need to be repeated every 6-12 months.

c. Sacral nerve stimulation:
Sacral nerve stimulation has been FDA approved for the therapy of refractory UUI since 1997 and refractory urgency/frequency since 1998. It is also approved for the treatment of idiopathic non-obstructive urinary retention and fecal incontinence. The mechanism of action is not fully understood. It involves a direct stimulation of the S3 sacral nerve by an electrode implanted percutaneously that is connected to an impulse generator located in the buttock area.

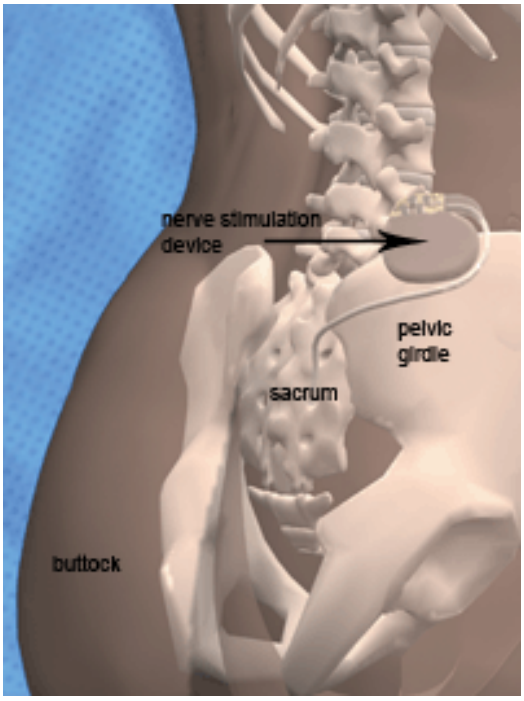

Figure 6. Sacral Nerve Stimulation, Medtronic 2016.

Patient cannot have a body MRI once the device is implanted. MRI of the head can be obtained. Revision of the device is also required in 25% of the time and the permanent generator needs to be changed every 3-5 years.

d. Augmentation cystoplasty:
This is the last resort option once everything else fails. It involves using a segment of bowel, usually the ileum or colon, and increasing the bladder capacity by connecting the segment of bowel to the bladder. It is a very invasive surgery and patients need to be able to self-catheterized after surgery.

III. Stress urinary incontinence
Stress urinary incontinence is the complaint of involuntary leakage on effort or exertion, or on sneezing or coughing or any activity that increases in intra-abdominal pressure. Stress incontinence is the most common type in younger women, with the highest incidence in women ages 45 to 49 years.

A. Causes of stress incontinence:
The main causes of SUI are urethral hypermobility and intrinsic sphincteric deficiency.

Urethral hypermobility is caused by insufficient support of the pelvic floor musculature and vaginal connective tissue to the urethra and bladder neck. This causes the urethra and bladder neck to lose the ability to completely close against the anterior vaginal wall. With increases in intra-abdominal pressure, the urethra fails to close, leading to incontinence. Deficient urethral support is related to pelvic muscles injury due to childbirth, vaginal deliveries, chronic cough, obesity or high-impact activities.

Intrinsic sphincteric deficiency (ISD) is another form of stress urinary incontinence that results from a loss of urethral tone that normally keeps the urethra closed. This can occur in the presence or absence of urethral hypermobility and typically results in severe urinary leakage even with minimal increases in abdominal pressure. In general, ISD results from neuromuscular damage and is usually seen in older patients, patients who have had multiple pelvic or incontinence surgeries or history of pelvic radiation.

B. Evaluation of stress incontinence:
The evaluation of patients with SUI is similar to patients with OAB syndrome. History and physical examination are necessary. According to the new AUA guidelines for the Evaluation and treatment of SUI, initial evaluation should include history, physical examination, demonstrated of SUI on exam, PVR assessment and Urinalysis.

1. History
Important elements to obtain from the patient's history are the presence of Sui symptoms, activities leading to SUI, severity and degree of bother, previous pelvic surgeries, OAB symptoms, difficulty emptying, hesitancy, fluid intake habit etc.

2. Physical Examination:
Physical examination including a pelvic examination should be performed to assess the presence of pelvic organ prolapse, urethral diverticulum, atrophic vaginitis, perineal sensation, pain and suprapubic distension.

-A supine stress test should also be performed, preferably with a full bladder, to assess the presence of SUI. Several protocols have been used to standardize this test. In general, patient should have 150-300cc in their bladder and asked to cough in supine position and observation of leakage should be noted. If no leakage is visualized, the stress test should be repeated in standing position.

3. Post-void residual: should be assessed in patients with obstructive symptoms, history of incontinence surgery, neurologic diseases and at the clinician discretion when PVR assessment is deemed necessary. It can be obtain using UA bladder scan or urethral catheter immediately after a patient voids.

4. Urodynamic study:
In cases where SUI was not demonstrated on examination, patients with significant mixed symptoms (both urgency and stress), obstructive voiding symptoms, elevated post void residual, history of neurologic diseases or history of anti-incontinence procedures, a urodynamic study should be obtain to confirm the presence of SUI, exclude possible bladder outlet obstruction and assess bladder emptying.

5. Other tests
Voiding diary, cystoscopy, voiding cystogram can be obtained is judged necessary by the physician.

C. Management of stress incontinence
Treatment options for SUI is usually separated in 2 categories: conservative vs surgical treatments.

1. Conservative treatment options

a. Medication
No medication has been approved for the treatment of SUI.

b. Weight loss
In randomized trial, 8% weight loss in obese women was proven to significantly reduce the number of SUI episodes.

c. Pelvic floor physical Therapy (PFPT):
More commonly known as “Kegel exercises”, PFPT has been proven in several RCTs to be very effective in the treatment of SUI. It involves contracting the pelvic floor muscles or levator to increase the urethral closure during stress or physical activities. It is much more successful when it is combined with other behavioral therapy like fluid management, timed voiding, delayed voiding etc.
A representative strengthening program for PFMT could include sets of 10 to 12 near-maximal contractions, with each contraction held 6 to 8 seconds with equivalent rest period and repeated three to five times per day, every other day.

d. Pessaries/vaginal inserts for SUI:
A pessary is a plastic device that is inserted in the vagina. It is most often used for the treatment of pelvic organ prolapse, but some pessaries have been designed to the treatment of SUI. These types have a knob that presses against the bladder neck, increasing the urethral pressure. An over-the-counter option exists now, Poise Impressa.

Figure 7. Stress incontinence pessary. Campbell-Walsh urology, 2012

2. Surgical treatments:
According to the new AUA guidelines, surgical treatments for SUI include bulking agents, midurethral sling (synthetic), autologous fascia pubovaginal sling and Burch colposuspension

a. Bulking agents
This procedure is usually done in the office and consists of a periurethral injection of a synthetic material via cystoscopy in order to improve the coaptation of the urethra. Durasphere EXP, Coaptite and Macroplastique are currently the available products and have similar efficacy. It has a high efficacy in patients with ISD. However, cure or improvement occurs in 70-80% but total continence has only been observed in 40% of patients. Repeat injection may also be required.

b. Mid-urethral sling
This surgery is now the procedure the most frequently performed for SUI. It involves placing a piece of synthetic (polypropylene mesh) material at the level of the mid-urethral via a small vaginal incision. Two different routes exist: retropubic or transobturator.

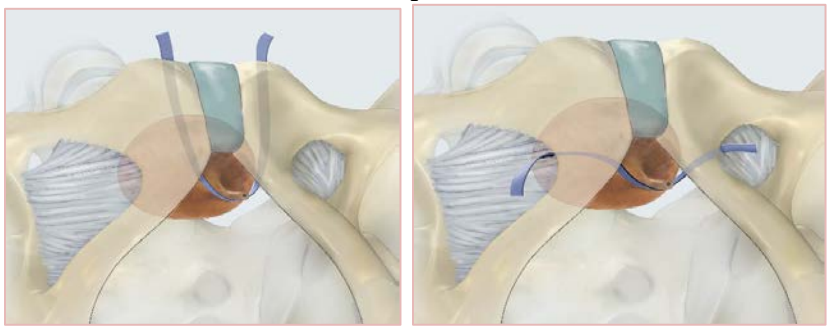

Figure 8. Retropubic mid-urethral sling Transobturator mid-urethral sling

This procedure is performed under local or general anesthesia and it is an outpatient procedure. It has high long term success rate. Success at 17 years of 92% was reported. Complications are usually mild and easily manageable. It treats both urethral hypermobility and ISD (especially retropubic). The main concern recently about these products has been related to the use of polypropylene mesh which has been associated with vaginal mesh extrusion, bladder perforation, pain and dyspareunia. However, multiple incision synthetic slings were “cleared” by the FDA in 2011.

c. Autologous fascia pubovaginal slings
This type of sling involves the placement of autologous material at the bladder neck. In addition to the correction of urethral hypermobility, the pubovaginal is also indicated for intrinsic sphincter deficiency associated with urethral hypermobility and SUI associated with urethral diverticulum or urethral defects (e.g., urethrovaginal fistula) in which urethral reconstruction is required and in women with SUI and associated neurogenic conditions.

It is also indicated for patients with recurrent SUI, who failed mid-urethral sling or bulking agents. The most commonly used autologous materials include rectus fascia and fascia lata. Rectus fascia is harvested through a suprapubic Pfannenstiel incision. The fascia lata can be harvested through a small incision on the side of the thigh. A vaginal incision is made at the level of the urethra and bladder, the endopelvic fascia is perforated and the bladder is completely freed from the retropubic space (urethrolysis). The fascia is then secured to sutures on both sides and brought via the vaginal incision to the retropubic space and the sutures are attaches loosely above the rectus fascia. Patients usually need to stay overnight after this surgery. It has a similar success rate than the mid-urethral sling but has a high rate of obstructive voiding symptoms.

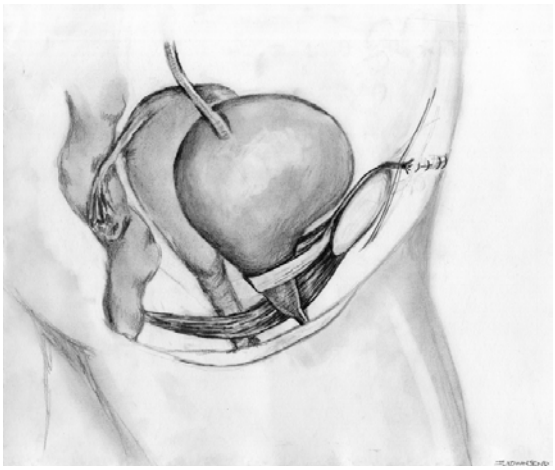

Figure 9. Placement of autolous pubovaginal sling and the bladder neck. Campbell-Walsh urology, 2012

d. Burch colposuspension Retropubic urethropexy

This surgery is a type of retropubic urethropexy to treat SUI secondary to urethral hypermobility. This is an open surgery which consists of lifting the tissue near the bladder neck and proximal urethra to the Cooper's ligament. It is performed very infrequently nowadays but can still be performed when it is combined to other laparoscopic or open repairs, like abdominal hysterectomy or prolapse repair.

An older similar procedure was the Marshall-Marchetti-Krantz (MMK). In this procedure, the proximal urethra is to the periostium of the pubic symphysis. Its success rate is usually poor and should not be offered nowadays. A rare but very serious complication that was specific to this procedure was osteitis pubitis.

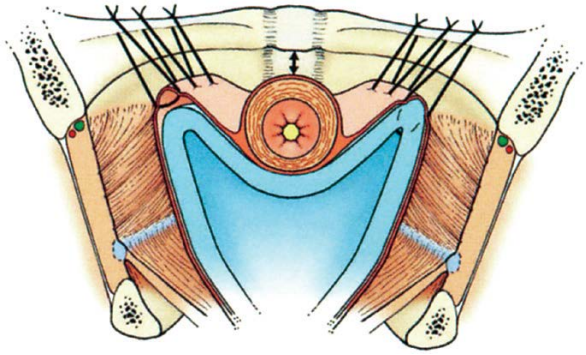

Figure 10. Burch colposuspension, Campbell-Walsh urology, 2012